REMARKS

Status of the Claims

Claims 1-116 were previously cancelled. Claims 126, 133, 138, 139, 142, 143 and 149-178 were previously withdrawn. Claims 117, 125, 147, and 148 have been amended. Claims 117-125, 127-132, 134-137, 140, 141, 144-148, and newly added claims 179-180 are currently pending.

Claim Rejection— 35 U.S.C. §112 ¶ 2

The Examiner asserts that independent claim 117 and dependent claims 118-125, 127-132, 134-137, 140, 141, and 144-148 fail to comply with the written description requirement, stating that "claim 117 does not limit a recipient polynucleotide as a double stranded nucleic acid." (Office Action, Pg. 4)

In response, Applicants have amended claim 117 to recite "recipient polynucleotide *duplex*." Applicants have also amended claim 117 to indicate that the displacer is introduced *to* the recipient polynucleotide duplex.

Support for these changes is found e.g. in the following section of the specification (Page 19, lines 17-24):

> One of the significant uses of our invention is for the site specific addition or deletion of nucleotides in a recipient polydeoxynucleotide sequence. This process occurs when the new strand is introduced to the recipient *duplex* and displaces the original strand. The cellular machinery involved in generalized recombination and gene conversion will act to transfer sequence information from the displacer *strand* to the recipient polydeoxynucleotide. (emphasis added).

In view of these changes, withdrawal of this rejection is respectfully requested.

Claim Rejection— 35 U.S.C. § 102(e)

The Examiner asserts that claims 117-119, 121, 125, 134-136, 144 and 145 are anticipated under 35 U.S.C. §102(e) by Lin *et al.* (U.S. Patent No. 5,214,136), citing three main reasons: (i) "the nucleic acid displacer taught by Lin *et al.* has an ability to changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide taught by Lin *et al.* when the displacer is introduced into the recipient polynucleotide"; (ii) "when the displacer is introduced into the recipient polynucleotide, the recipient polynucleotide recited in claim 117 is not part of a nucleic acid displacer composition"; and (iii) "the phrase 'wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide nucleotide' recited in claim 117 is not a structural limitation of the claim, but is a functional limitation of the claim." (Office Action, Pgs. 8-9)

The amended claims of the instant application are all drawn to a nucleic acid displacer composition, which comprises an isolated displacer that binds to or complexes with a recipient polynucleotide *duplex* to form a displacer-recipient complex. The displacer-recipient complex forms such that the oligo- or polynucleotide displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex. The "displacer" is not "introduced *into* the recipient polynucleotide" as suggested above. Rather the displacer is introduced *to* the recipient polynucleotide and has characteristics allowing it to form a displacer-recipient complex that leads to displacing an original strand, binding the other one strand, and ultimately changing at least one nucleotide or a nucleotide sequence in the recipient polynucleotide duplex.

These required functional characteristics are specific properties of the claimed displacer compositions. Lin *et al.* however, provides no indication that the oligomers disclosed therein have any of these characteristics or properties. The oligomers in Lin *et al.* "are characterized by their ability to target specific oligonucleotide sequences regardless of the mechanisms of targeting or the mechanism of the effect thereof." (Col. 6, ll. 18-21). There is no disclosure or suggestion in Lin *et al.* that the disclosed oligomers are able to form a displacer-recipient complex. Nor does Lin *et al.* teach or suggest a nucleic acid molecule that is able to displace one strand in a recipient polynucleotide duplex and bind to the other.

Instead, Lin *et al.* discloses that "the mechanism by which the specifically-binding oligomers of the invention interfere with or inhibit the activity of a target RNA or DNA is not always established, and is not a part of the invention." (Col. 6, ll. 1-5). In fact, the only mention of functional characteristics for oligomers in Lin *et. al.* are binding an mRNA target, forming a triple helix, and interfering with reverse transcription -- none of which necessarily mean strand displacement. (Col. 6, ll. 6-17). Lin *et al.* provides no indication to one skilled in the art that the oligomers will have the functional characteristics required in the claims of the instant application. *See* M.P.E.P. § 2173.05 ("A functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used.")

Since "[a]nticipation under 35 U.S.C. §102 requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention," Electro Med. Sys. S.A. v. Cooper Life Sciences, 32 U.S.P.Q.2d 1017, 1019 (Fed. Cir. 1994), Applicants respectfully submit that Lin *et al.*, fails to meet the limitations of the instant claims.

In view of the foregoing, Applicants respectfully request withdrawal of the §102(e) rejection. Accordingly, withdrawal of the rejection is respectfully requested.

Claim Rejections — 35 U.S.C. § 103

Rejection of claims 146 and 147 as being obvious over Lin *et al.* further in view of Dattagupta *et al.* (U.S. Patent No. 4,737,454)

Three basic criteria must be met to support a *prima facie* case of obviousness: (a) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine the reference(s) teachings; (b) there must be a reasonable expectation of success; and (c) the prior art reference (or references when combined) must teach or suggest all the claim features. M.P.E.P. § 2143.

In this Office Action, the Examiner sustained his rejection of claims 146 and 147, repeating the three reasons cited with respect to the §102(e) rejection above, and reasserting that "there is a motivation to combine the references from Lin *et al.*, and Dattagupta *et al.*

Applicants respectfully assert that Lin *et al.* and Dattagupta *et al.* do not individually or in combination suggest to a person of ordinary skill in the art the invention of the Applicants' claims 146 and 147, as these claims now incorporate the limitations from amended claim 117.

Neither Lin *et al.* nor Dattagupta *et al.* teaches or suggests oligo- or polynucleotides that are able to form a complex with a polynucleotide duplex, resulting in displacement of one strand and binding to the other. Nor is this teaching covered by the Examiner's assertion that "Lin *et al.* do teach said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide recited in the claim" (Office Action, Pg. 13) While Lin *et al.* teaches a duplex comprising an RNA target and an mutated oligomer, this is <u>not</u> a displacer-recipient complex. Such a complex requires a third component missing in Lin *et al*: a second strand in the recipient polynucleotide duplex that would be specifically displaced by the oligomer. No such showing is made or suggested in Lin *et al.*

Accordingly, even if one *were* to combine Dattagupta *et al.* and *Lin* et al., the result would only be nucleic acid compositions having additional moieties, such as "phosphorothioate linkages and antigens as recited in claim 146 and a modification which allows capture of the displacer-recipient complex by affinity chromatography as recited in claim 147." (Office Action, Pg. 10). These references would not teach or suggest the nucleic acid displacer composition required in the claims.

In view of the foregoing, Applicants respectfully request withdrawal of the §103 rejection in this section..

<u>Rejection of claim 148 as being obvious over *Lin* et al.</u>

In this section, the Examiner purports that "there is a motivation to alter the Lin *et al.*, displacer to form an artificially constructed polynucleotide comprising a naturally occurring recipient polynucleotide duplex hybrid[ized] to the nucleic acid displacer composition." (Office Action, Pages 15-16) According to the Examiner, "[o]ne having ordinary skill in the art would have been motivated to do so because Lin *et al.* tested the oligonucleotide coupled to anthraquinone *in vitro* and *in vivo* and hybridized the oligonucleotide coupled to

anthraquinone to a single stranded RNA and one having ordinary skill in the art would select a hybridized target nucleic acid such as naturally occurring RNA based on his or her experimental requirements." (Office Action, Pg. 14)

But the resulting complex, as described by the Examiner, would not meet all the limitations required in dependent claim 148, which includes all limitations in base claim 117. As discussed in this response, the nucleic acid displacer composition of claim 117 includes the properties that it displaces one strand in the target *duplex* and binds to the other. No target duplex -- and hence no displacement -- is disclosed in the complex envisaged by the Examiner. This argument also rests on the unfounded premise that such a displacer would change a nucleotide or nucleotide sequence in an RNA strand.

In view of the foregoing, Applicants respectfully request withdrawal of the §103 rejection in this section.

CONCLUSION

An indication of allowance of all claims is respectfully solicited. Early notification of a favorable consideration is respectfully requested. In the event any issues remain, Applicants would appreciate the courtesy of a telephone call to their counsel to resolve such issues and place all claims in condition for allowance.

This paper has been filed with a Request for Continued Examination (RCE). The Commissioner is hereby authorized to charge $405.00 from the undersigned's **Deposit Account No. 50-0206** to cover the RCE fee for a small entity. It is believed that no additional fees are required with this submission. However, in the event that any variance in these fees are determined, please charge or credit any such variance to the undersigned's Deposit Account No. 50-0206.

Respectfully submitted,

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